Case report

Tezepelumab achieves improvement of severe uncontrolled asthma and rhinosinusitis: Case series

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Tezepelumab, a mAb targeting thymic stromal lymphopoietin (TSLP), reduces exacerbations in severe asthma. Four cases in which patients with severe asthma and chronic rhinosinusitis with nasal polyps showed improvements in both conditions after receiving tezepelumab treatment are presented. (J Allergy Clin Immunol Global 2025;4:100448.)

Key words: *Asthma control, tezepelumab, rhinosinusitis, severe asthma, nasal polyps*

Abbreviations used

CRSwNP:	Chronic rhinosinusitis with nasal polyps
CT:	Computed tomography
FENO:	Fractional exhaled nitric oxide
%FEV_1:	Percent predicted FEV_1 value
FEV_1/FVC:	Ratio of FEV_1 value to forced vital capacity
ICS:	Inhaled corticosteroid
LABA:	Long-acting β-agonist
LAMA:	Long-acting antimuscarinic agent
LMCT:	Lund-Mackay computed tomography
OCS:	Oral corticosteroid
PFT:	Pulmonary function testing
TSLP:	Thymic stromal lymphopoietin

Asthma and chronic rhinosinusitis with nasal polyps (CRSwNP) are frequently associated.[1,2] Approximately 40% of individuals with severe asthma are estimated to have CRSwNP,[3] and patients with asthma and CRSwNP tend to experience worse symptoms in their sinuses and nose as well as increased inflammation in the lower respiratory tract. Additionally, these patients may have impaired lung function and lower quality of life.[4] Moreover, two-thirds of patients with CRSwNP have asthma,[5] and these patients exhibited more severe nasal obstruction, a higher chance of a recurrence of nasal polyps even after surgery, difficulty in managing their asthma, and significant impairment of quality of life.[6] Patients with both diseases are often difficult to treat, and the economic impact of the illness on patients of both conditions has been noted.[7]

Thymic stromal lymphopoietin (TSLP) is a cytokine secreted by epithelial cells[8,9]; it is considered to be involved in the pathogenesis of both type 2– and non–type 2–mediated asthma, contributing to the initiation and maintenance of airway inflammation. Tezepelumab, a human mAb that binds to TSLP, prevents the TSLP molecule from attaching to its heterodimeric receptors, and it reduces exacerbations in adults with severe uncontrolled asthma.[10]

Here, we report a first case series of 4 patients with severe asthma concomitant with CRSwNP at 3 different medical centers, in which both asthma and CRSwNP were improved after treatment with tezepelumab. All of the participants gave written informed consent.

Case patient 1, a 57-year-old male, was diagnosed with asthma 7 years ago and treated with an inhaled corticosteroid (ICS)/long-acting β-agonist (LABA) (budesonide/formoterol, 200/6 μg; 4 inhalations twice daily) and long-acting antimuscarinic agent (LAMA) (tiotropium, 5 μg once daily). However, he experienced repeated asthma attacks with CRSwNP exacerbations (Fig 1, *A*), requiring burst uses of oral corticosteroids (OCSs) for 3 years. CRSwNP was diagnosed with eosinophilic sinusitis after a biopsy of nasal polyps. Blood tests showed eosinophilia (12.1% [620 cells/μL]) and a high level of IgE (2129 IU/mL). Pulmonary function testing (PFT) indicated a percent predicted FEV_1 value (%FEV_1) of 70.8%, ratio of FEV_1 value to forced vital capacity (FEV_1/FVC) of 62.9%, and FENO level of 74 ppb (see Fig E1 in the Online Repository at www.jaci-global.org), as a result of which he underwent mepolizumab therapy. Although both his nasal and respiratory symptoms improved (Fig 1, *B*), they were aggravated 2 years after initiation of the mepolizumab (Fig 1, *C*). Mepolizumab was switched to dupilumab. The patient's symptoms were temporarily suppressed (Fig 1, *D*) but worsened again a month later (Fig 1, *E*), resulting in the need for an OCS

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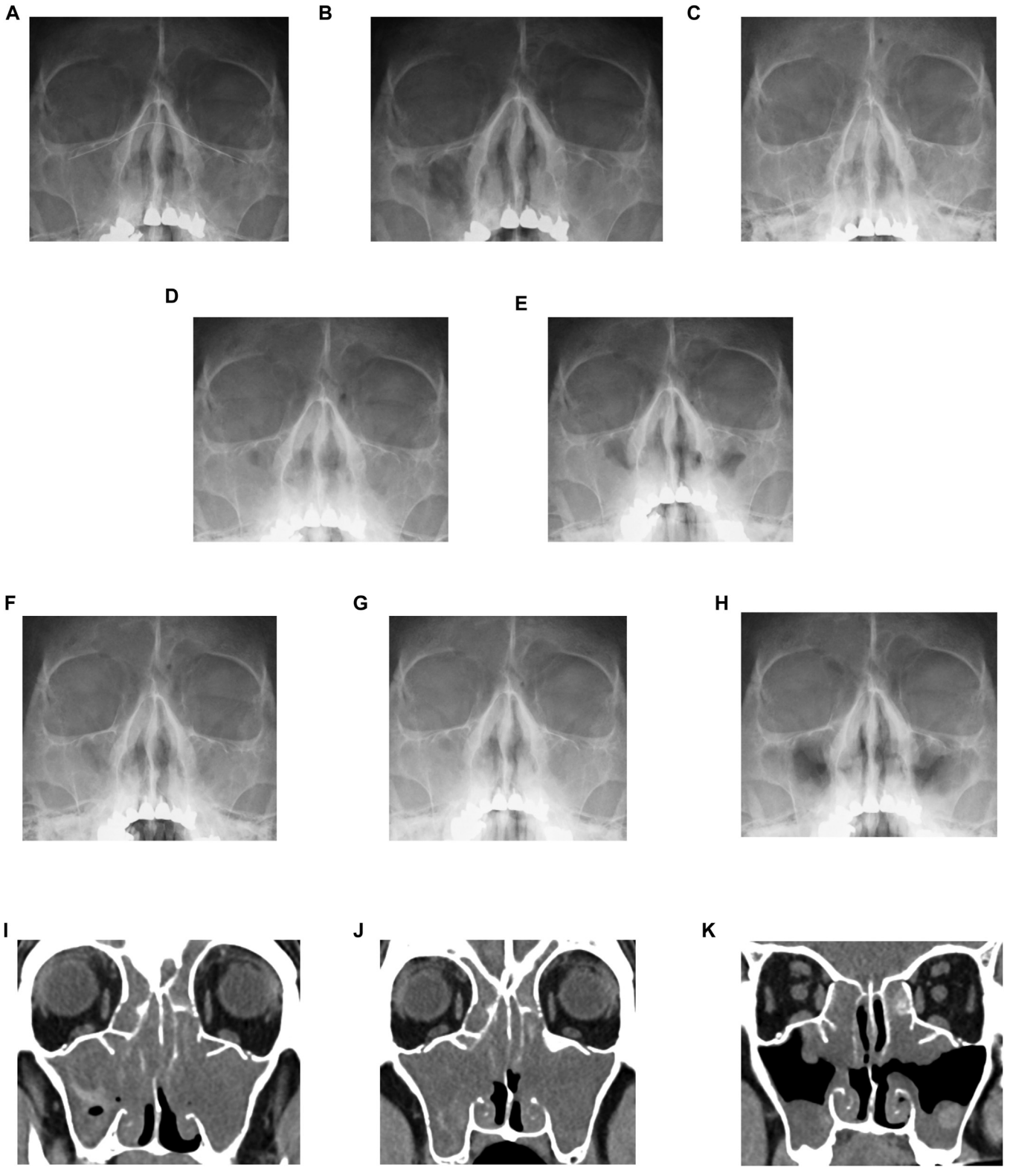

FIG 1. Waters radiographic views CT in case 1. **A** and **B,** Views before the start of mepolizumab administration (**A**) and 2 months later (**B**); increased permeability of the right maxillary sinus is seen. **C** and **D**, Views before the switch to dupilumab (**C**) and 2 weeks later (**D**); slightly increased permeability of both maxillary sinuses is seen. **E,** Five weeks after the start of dupilumab, diffusive decreased permeability in sinuses is seen. **F** and **I,** Worsening after the switch to benralizumab and soft shadow filling of the ethmoid and maxillary sinuses were seen. **G, H, J,** and **K,** After administration of tezepelumab, CT scans showed improvement of the ethmoid and maxillary sinuses.

short burst. Repeat administration of mepolizumab did not improve CRSwNP (Fig 1, *F* and *I*); as a result, prednisolone was restarted at a rate of 30 mg per day. The prednisolone dose could not be reduced below 10 mg/day; therefore, mepolizumab was switched to benralizumab. Prednisolone was tapered to 2.5 mg/day over 6 months. Two months later, however, he had another asthma attack requiring OCS burst, and tezepelumab was subsequently administered. One month later, prednisolone was safely tapered off. Improvements in both symptoms and computed tomography (CT) findings of CRSwNP were observed 5 months after the initiation of tezepelumab treatment (Fig 1, *G*, *H*, *J*, and *K*); in addition, the patient's Lund-Mackay CT (LMCT) score also improved (from 12 on X-1/8 to 6 on X/2).

Case patient 2 was a 72-year-old male who was referred to a core hospital in March because of poor control of his asthma symptoms. He had been diagnosed with asthma 4 years earlier, was being treated with an ICS/LABA/LAMA (fluticasone furoate, 100 μg; vilanterol, 25 μg; and umeclidinium, 62.5 μg), and was taking reliever salbutamol inhalation daily. He had a total of 4 asthma attacks over the past 2 years, each time taking the OCS for several days. His nasal symptoms were treated with a fluticasone furoate nasal spray. PFT indicated a %FEV_1 value of 73.0%, FEV_1/FVC value of 63.1%, and FENO level of 56 ppb. A CT scan showed soft shadow filling of the bilateral ethmoid and maxillary sinuses (Fig 2, *A*). Blood tests showed eosinophilia (21.4% [1800 cells/μL]) and a high level of IgE (498 IU/mL). After a biopsy of his nasal polyps, he was diagnosed with severe eosinophilic sinusitis. His inhalation treatment was escalated to high-dose ICS/LABA/LAMA (fluticasone furoate, 200 μg), after which his symptoms improved but worsened in June on account of a respiratory infection, resulting in cough and nasal obstruction. He was given a short-term OCS burst and began receiving tezepelumab, after which the OCS was no longer needed. His nasal symptoms gradually improved. His FENO level showed a continuous decrease (see Fig E2, *A* in the Online Repository at www.jaci-global.org), a CT scan in October showed improvement (Fig 2, *B*), and his LMCT score was also improved (from 17 on X/3 to 10 on X/10).

Case patient 3 was a 74-year-old male who was referred to a core hospital in August for repeated asthma attacks; he was administered prednisolone, 10 mg every day. He also had nasal congestion and nasal polyps. The patient's laboratory data included a peripheral blood eosinophil count of 39 cells/μL and IgE level of 518 IU/L. PFT indicated a %FEV_1 value of 33%, FEV_1/FVC value of 45.3%, and FENO level of 118 ppb. A CT scan exhibited mucosal thickening within the left ethmoid sinus (Fig 2, *C*). Inhalants of an ICS/LABA (budesonide/formoterol, 200/6 μg; 4 inhalations twice daily) and LAMA (tiotropium, 5 μg twice daily) had been administered by the previous clinic. An increase in FEV_1 value and a decrease in FENO level were seen in September (see Fig E2, *B*). Tezepelumab treatment was started in October because the OCS could not be tapered off. The patient's respiratory and nasal symptoms were improved, and the OCS was gradually tapered and then discontinued after 3 months. Mucosal thickening of the ethmoid sinus had also improved on the patient's recent CT scan (Fig 2, *D*), and the patient's LMCT score was also improved, from 5 on X/8 to 3 on X+1/1.

Case patient 4, a 69-year-old female, was treated for asthma with an ICS/LABA (budesonide/formoterol, 200/6 μg; 4 inhalations twice daily), LAMA (tiotropium, 5 μg once daily), and montelukast in a core hospital after being referred for poorly controlled asthma. Her respiratory symptoms were stable, but she had asthma attacks several times in June, each of which was treated with a short-term OCS. She also complained of some nasal symptoms. A CT scan showed soft shadow bilateral filling of the ethmoid and maxillary sinuses (Fig 2, *E*). PFT indicated a %FEV_1 value of 65.7%, FEV_1/FVC value of 58.9%, and FENO level of 55 ppb. Blood tests showed eosinophilia (9.3% [760 cells/μL]) and a high level of IgE (470 IU/mL). After she had started taking tezepelumab, her respiratory and nasal symptoms improved, she had no subsequent asthma attacks, and a CT scan performed 6 months after she had started taking tezepelumab showed improvement in soft tissue shadows (Fig 2, *F*). Furthermore, her PFT results were improved as well (see Fig E2, *C*), and her LMCT Score[11] was also improved (14 on X/8 to 6 on X+1/1).

The present case series demonstrates that tezepelumab can control both asthma and CRSwNP by suppressing type 2 inflammation. It was reported that patients with CRSwNP had strong type 2 inflammation[12] and elevated expression of TSLP on polyps.[13] In addition, increased TSLP expression was seen more often in patients with asthma than in healthy controls, and it was interrelated with the expression of type 2 cytokines and chemokines,[14] as well as with the severity of asthma.[15,16] Tezepelumab specifically targets TSLP, and a pivotal phase III study of patients with atopic asthma demonstrated that tezepelumab could effectively control both early and late asthmatic responses.[17] The Visual Analog Scale scores of nasal obstruction and smell, as well as loss of smell score, showed improvement in case patients 2 to 4 (see Table E1 in the Online Repository at www.jaci-global.org). The patient's symptoms of CRSwNP had been stable under tezepelumab treatment, but we have observed the patients for a only maximum of 10 months. It would be necessary to observe both subjective symptoms and objective findings regarding CRSwNP over a long period of time. Several biologic agents for severe uncontrolled asthma, including omalizumab, mepolizumab, benralizumab, dupilumab, and tezepelumab, are currently available in Japan. However, when the patients in this case series began taking tezepelumab, dupilumab was the only biologic agent approved for CRSwNP in Japan. For case patients 2, 3, and 4, tezepelumab was selected as the initial biologic treatment on the basis of multiple positive biomarkers, including total IgE level and patient preferences regarding dosing intervals. Further studies of the efficacy of tezepelumab in these patients are warranted.

In conclusion, this case series reveals a novel aspect of tezepelumab, controlling both severe asthma and rhinosinusitis. When patients with asthma or rhinosinusitis are seen, confirming the presence or absence of both complications may be important in selecting active candidates for tezepelumab administration.

DISCLOSURE STATEMENT

Disclosure of potential conflict of interest: K. Tanaka received payments for lectures from AstraZeneca and Novartis. H. Inoue received payments for lectures or advisory committees from AstraZeneca, Boehringer-Ingelheim, Kyorin, GlaxoSmithKline, Novartis, and Sanofi, as well as grants from Boehringer-Ingelheim, GlaxoSmithKline and Omuron. The rest of the authors declare that they have no relevant conflicts of interest.

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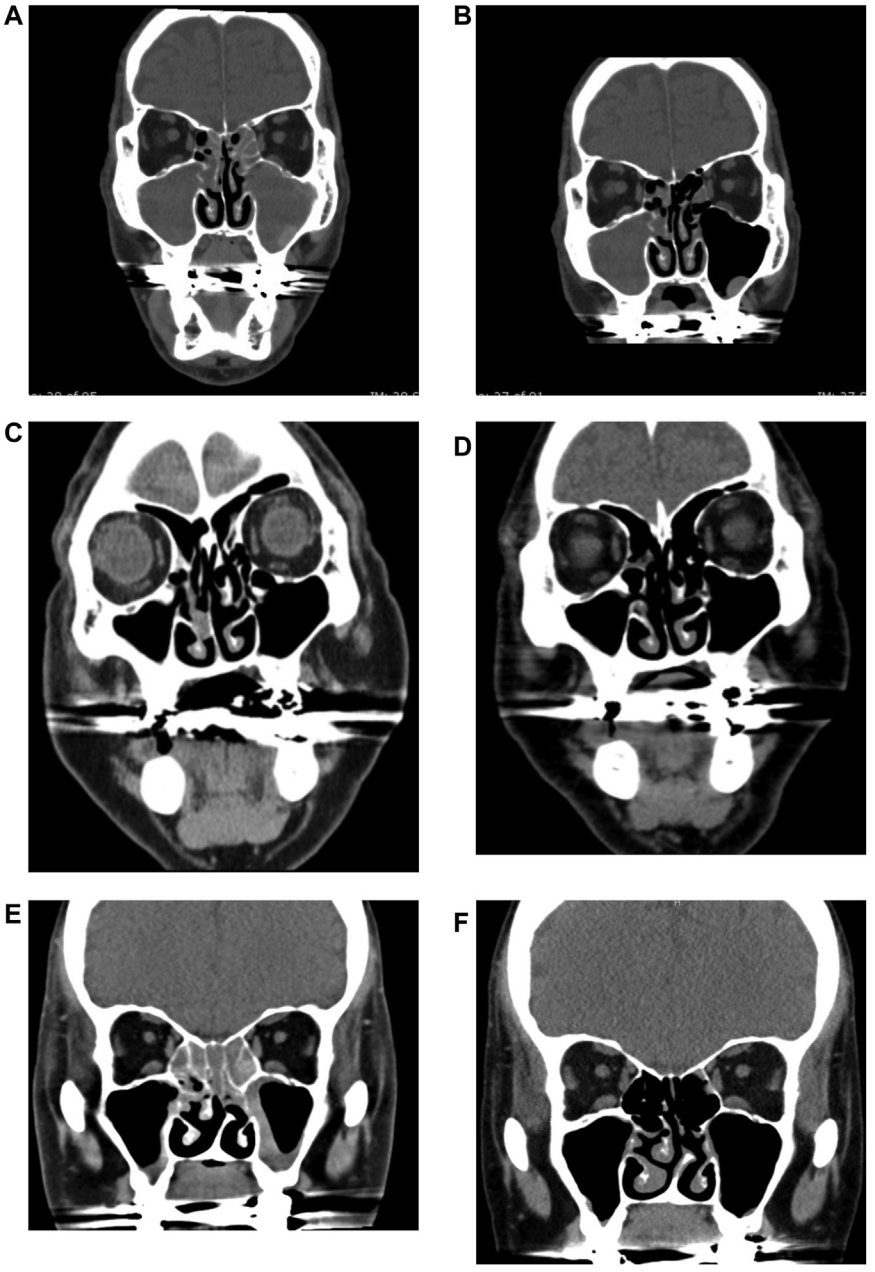

FIG 2. The CT scan findings regarding case patients 2 to 4. **A** and **B,** CT scans of case patient 2 showing soft shadow filling of the bilateral ethmoid and maxillary sinuses in the referred hospital before administration of tezepelumab in March (**A**); after administration of tezepelumab, improvement was seen in the soft tissue shadows of the ethmoid and maxillary sinuses in October (**B**). **C** and **D,** CT scans of case patient 2 showing mucosal thickening within the left ethmoid sinus in the referred hospital before administration of tezepelumab in August (**C**); after tezepelumab therapy was started, improvement was seen in the soft tissue shadows of the ethmoid sinuses in January (**D**). **E** and **E,** CT scans of case patient 4 show soft tissue shadow bilateral filling of the ethmoid and maxillary sinuses in June (**E**); after the start of tezepelumab therapy, improvement was seen in both sinuses in January (**F**).

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